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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/063,514	05/01/2002	Dan L. Eaton	10466/299	8123

30313 7590 09/08/2004

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EXAMINER

ROMEO, DAVID S

ART UNIT	PAPER NUMBER
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1647

DATE MAILED: 09/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/063,514

Applicant(s)

EATON ET AL.

Examiner

David S Romeo

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 September 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 09/10/2002.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

The preliminary amendment filed 09/09/2002 has been entered. Claims 1-13 are pending and being examined.

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Priority

The present application is claiming priority under 35 U.S.C. 120 and 119 (e) to earlier filed applications. Under 35 U.S.C. 120, the claims in a U.S. application are entitled to the benefit of the filing date of an earlier filed U.S. application if the subject matter of the claim is disclosed in the manner provided by 35 U.S.C. 112, first paragraph in the earlier filed application. Under 35 U.S.C. 119 (e), the claims in a U.S. application are entitled to the benefit of a foreign priority date or the filing date of a provisional application if the corresponding foreign application or provisional application supports the claims in the manner required by 35 U.S.C. 112, first paragraph. A deficiency under 35 U.S.C. 101 also creates a deficiency under 35 U.S.C. 112, first paragraph.

15 The presently claimed invention lacks utility for the reasons set forth in the rejections below. Hence, neither the present application nor any of the other earlier filed applications provide a disclosure in the manner provided by 35 U.S.C. 112, first paragraph. Accordingly, the effective filing date of the presently claimed compounds is 05/01/2002, which is the filing date of the present application.

20

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

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Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

10

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-13 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

15

The claims are directed to or encompass polypeptides having at least 80% identity to the PRO874 polypeptide (SEQ ID NO: 10) or some portion thereof. The present application characterizes the PRO874 polypeptide and polynucleotide as follows:

20

[0036] FIG. 9 shows a nucleotide sequence (SEQ ID NO: 9) of a native sequence PRO874 cDNA, wherein SEQ ID NO: 9 is a clone designated herein as "DNA40621-1440".

[0037] FIG. 10 shows the amino acid sequence (SEQ ID NO: 10) derived from the coding sequence of SEQ ID NO: 9 shown in FIG. 9. Page 11.

25

DNA40621-1440 is more highly expressed in normal lung than as compared to lung tumor. Example 18, Page 141.

30

Figure 10 also provides various structural features of the PRO874 polypeptide, presumably based on homology with domains of other known proteins. It is noted that PRO874 is less than a full length polypeptide because the amino acid sequence of SEQ ID NO: 10 does not begin with an initiator methionine. No further characterization is provided.

The tumor versus normal differential tissue expression distribution (Example 18) provides only a use for a limited number of nucleic acid probes. No information is provided in the differential tissue expression distribution data regarding the level of expression, activity, or role in cancer of the PRO874 polypeptide. Further, differential tissue nucleic acid expression is not always correlated with protein levels. For example, Allman (U) discloses that germinal center B cells express dramatically more BCL-6 protein than resting B cells, despite similar BCL-6 mRNA levels in the two cell populations. Page 5257, paragraph bridging left and right columns. mRNA translation is regulated in many genes and can be mediated by binding of proteins to cis-acting RNA motifs in the untranslated regions of the mRNAs (paragraph bridging pages 5266-5267).

Furthermore, one skilled in the art recognizes that although structural similarity can serve to classify a protein as related to other known proteins this classification is insufficient to establish a function or biological significance for the protein because ancient duplications and rearrangements of protein-coding segments have resulted in complex gene family relationships. Duplications can be tandem or dispersed and can involve entire coding regions or modules that correspond to folded protein domains. As a result, gene products may acquire new specificities, altered recognition properties, or modified functions. Extreme proliferation of some families within an organism, perhaps at the expense of other families, may correspond to functional innovations during evolution. See Henikoff (V), page 609, Abstract. Accordingly, one skilled in the art would not accept mere homology as establishing a function of protein because gene products may acquire new specificities, altered recognition properties, or modified functions. Rather, homology complements experimental data accumulated for the homologous protein in

understanding the homologous protein's biological role. Although, the presence of a protein module in a protein of interest adds potential insight into its function and guides experiments, insight into the biological function of a protein cannot be automated. However, homology can be used to guide further research. See Henikoff (V), paragraph bridging pages 613-614, through
5 page 614, paragraph bridging columns 1-2.

The instant claims encompass a protein of as yet undetermined function or biological significance. Until some actual and specific significance can be attributed to the protein identified in the specification as PRO874 one of ordinary skill in the art would be required to perform additional experimentation in order to determine how to use it. Thus, there was no
10 immediately apparent or "real world" utility for the PRO874 polypeptide as of the filing date.

After further research, a specific and substantial utility might be found for the PRO874 polypeptide of the instant invention. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete.

15 Claims 1-13 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

20 ***Claim Rejections - 35 USC § 112***

Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in

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the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to polypeptides having at least 80% amino acid sequence identity to the polypeptide of SEQ ID NO: 10, to said polypeptide lacking its associated signal peptide, or
5 to the extracellular domain thereof. There is no functional limitation in the claims.

The claim encompasses an unreasonable number of inoperative polypeptides, which the skilled artisan would not know how to use. While the specification suggests that the polypeptide of SEQ ID NO: 10 is a membrane bound polypeptide, membrane bound polypeptides have widely varying activities. See paragraph bridging pages 3-4. Therefore, knowledge that a protein
10 is a membrane bound polypeptide does not provide predictability about function of that protein or a structurally related protein.

There are no working examples of polypeptides less than 100% identical to SEQ ID NO: 10. The skilled artisan would not know how to use non-identical polypeptides on the basis of teachings in the prior art or specification unless they possessed some disclosed function. The
15 specification does not provide guidance for using polypeptides related to (i.e., 80%-99% identity) or identical to SEQ ID NO: 10. The claims are also broad because they do not require the claimed polypeptide to be identical to the disclosed sequence and because the claims have no functional limitation.

Moreover, there is a lack of predictability in the art. Predicting structure, hence function,
20 from primary amino acid sequence data is extremely complex and there doesn't exist an efficient algorithm for predicting the structure of a given protein from its amino acid sequence alone. See

Bowie (X) page 1306, column 1, full paragraph 1, and Ngo (Y) page 433, full paragraph 1, and page 492, full paragraph 2.

For these reasons, which include the complexity and unpredictability of the nature of the invention and art in terms of the diversity of secreted proteins and lack of knowledge about function(s) of encompassed polypeptides structurally related to SEQ ID NO: 10, the lack of working example of PRO874 polypeptide and its function, the lack of direction or guidance for using polypeptides that are not identical to SEQ ID NO: 10, and the breadth of the claims for structure without function, it would require undue experimentation to use the invention commensurate in scope with the claims.

Claims 1-13 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to polypeptides having at least 80%, 85%, 90%, 95% or 99% sequence identity with a particular disclosed sequence. The claims do not require that the polypeptide possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polypeptides that is defined only by sequence identity. It is noted that PRO874 is less than a full length polypeptide because the amino acid sequence of SEQ ID NO: 10 does not begin with an initiator methionine.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus.

The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is not even

5 identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in
10 possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed.” (See page 1117.) The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See Vas-Cath at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical
15 structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai
Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

20 One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481 at 1483. In Fiddes, claims directed to mammalian FGF's were found to be unpatentable due to

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lack of written description for that broad class. The specification provided only the bovine sequence.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

5

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10 Claims 1-6, 8, 10, 12, 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1-6, 8, 10, 12, 13 are indefinite over the recitation of “signal peptide” because there is a lack of antecedent basis in the specification for the signal peptide of SEQ ID NO: 10. It is further noted that PRO874 is less than a full length polypeptide
15 because the amino acid sequence of SEQ ID NO: 10 does not begin with an initiator methionine. Thus, it is not even clear that the amino acid sequence of SEQ ID NO: 10 has a signal peptide. The metes and bounds are not clearly set forth.

 Claims 1-6, 9, 10, 12, 13 are rejected under 35 U.S.C. 112, second paragraph, as being
20 indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1-6, 9, 10, 12, 13 are indefinite over the recitation of “the extracellular domain.” There is a lack of antecedent basis in the specification for “the extracellular domain.” Figure 10 discloses that SEQ ID NO: 10 possesses several transmembrane domains, and, thus, a corresponding number of extracellular domains, depending

5 extracellular domains as “the extracellular domain” it is unclear if all of “the extracellular domain” is disclosed. The metes and bounds are not clearly set forth.

Claim Rejections - 35 USC § 102

10 basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15 Claims 1-13 rejected under 35 U.S.C. 102(b) as being anticipated by Baker (N). This rejection is based upon an effective filing date of 05/01/2002, the filing date of the present application, for the presently claimed compounds. Baker discloses an isolated polypeptide (page 55, full paragraph 4) that is identical to the amino acid sequence of SEQ ID NO: 10, as indicated below (Qy = SEQ ID NO: 10):

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20      Query Match          100.0%;   Score 1709;   DB 21;   Length 321;
      Best Local Similarity 100.0%;   Pred. No. 2.4e-181;
      Matches 321;   Conservative    0;   Mismatches    0;   Indels    0;   Gaps    0;

25      Qy      1      RTRGRTRGGCEKVPINTSCNPTAHLVNSSCPGLMCVFQGYSSKGLIQRSVFNLQIYGVLG 60
      Db      1      RTRGRTRGGCEKVPINTSCNPTAHLVNSSCPGLMCVFQGYSSKGLIQRSVFNLQIYGVLG 60
      |||||||
30      Qy      61      LFWTLNWLVALGQCVLGAFASFYWAFHKPDIPTFPLISAFIRTLRYHTGSLAFGALIL 120
      Db      61      LFWTLNWLVALGQCVLGAFASFYWAFHKPDIPTFPLISAFIRTLRYHTGSLAFGALIL 120
      |||||||

35      Qy      121     TLVQIARVILEYIDHKLRGVQNPVARCIMCCFKCCLWCLEKFIKFLNRRNAYIMIAIYGKN 180
      Db      121     TLVQIARVILEYIDHKLRGVQNPVARCIMCCFKCCLWCLEKFIKFLNRRNAYIMIAIYGKN 180
      |||||||

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5 QY 181 FCVSAKNAFMLLMRNIVRVVLDKVTDLLFFGKLLVVGGVGVLSFFFFSGRIPGLGKDF 240
Db 181 FCVSAKNAFMLLMRNIVRVVLDKVTDLLFFGKLLVVGGVGVLSFFFFSGRIPGLGKDF 240
10 QY 241 KSPHLNYYWLPIMTSILGAYVIASGFFSVFGMCVDTLFLCFLEDLERNNGSLDRPYYSK 300
Db 241 KSPHLNYYWLPIMTSILGAYVIASGFFSVFGMCVDTLFLCFLEDLERNNGSLDRPYYSK 300
QY 301 SLLKILGKKNEAPPDNKKRKK 321
Db 301 SLLKILGKKNEAPPDNKKRKK 321.

Baker also discloses a chimeric polypeptide comprising the isolated polypeptide fused to heterologous polypeptide wherein the heterologous polypeptide is an epitope tag or a Fc region of an immunoglobulin (page 280, lines 32-35).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

20 (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

25 Claims 1-4, 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over TrEMBL protein sequence database accession no. Q9Y332 (W) in view of Sibson (O).

This rejection is based upon an effective filing date of 05/01/2002, the filing date of the present application, for the presently claimed compounds. TrEMBL discloses the translation of a coding sequence, which is 97.5% identical to SEQ ID NO: 10, as indicated below (Db = TrEMBL translation):

35 Query Match 97.5%; Score 1667; DB 4; Length 712;
Best Local Similarity 100.0%; Pred. No. 3.1e-144;
Matches 313; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
QY 9 GCEKVPINTSCNPTAHLVNSSCPGLMCFVFGYSSKGLIQRSVFNLQIYGVLGLFWTLNWV 68
|||||

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Db 400 GCEKVPINTSCNPTAHLVNSSCPGLMCVFGYSSKGLIQRSVFNLQIYGVLGFWTLNWV 459
 QY 69 LALGQCVLGAFASFYWAFHKPDIPFTPLISAFIRTLRYHTGSLAFGALILTLVQIARV 128
 5 Db 460 LALGQCVLGAFASFYWAFHKPDIPFTPLISAFIRTLRYHTGSLAFGALILTLVQIARV 519
 QY 129 ILEYIDHKLRGVQNPVARCIMCCFKCCLWCLEKFIKFLNRNAYIMIAIYGKNFCVSAKNA 188
 10 Db 520 ILEYIDHKLRGVQNPVARCIMCCFKCCLWCLEKFIKFLNRNAYIMIAIYGKNFCVSAKNA 579
 QY 189 FMLLMRNIVRVVLDKVTDLLFFGKLLVVGGVGVLSFFFFSGRIPGLGKDFKSPHLNYY 248
 Db 580 FMLLMRNIVRVVLDKVTDLLFFGKLLVVGGVGVLSFFFFSGRIPGLGKDFKSPHLNYY 639
 15 QY 249 WLPIMTILGAYVIASGFFSVFGMCVDTLFLCFLEDLERNNGSLDRPYMSKSLKILGK 308
 Db 640 WLPIMTILGAYVIASGFFSVFGMCVDTLFLCFLEDLERNNGSLDRPYMSKSLKILGK 699
 20 QY 309 KNEAPPDNKKRKK 321
 Db 700 KNEAPPDNKKRKK 712.

TrEMBL does not disclose an isolated protein. However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to express and isolate the encoded protein, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to make this modification for structure function analysis of the encoded polypeptide. See for Sibson at page 10, line 38, through page 11, line 15. Sibson also suggest making a fusion/chimeric polypeptide (page 11, full paragraph 1). It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to express and isolate the polypeptide encoded by TrEMBL, as taught by TrEMBL, and to modify that teaching make a fusion polypeptide, as taught by Sibson, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to make this modification in order isolate or stabilize the expressed polypeptide. The invention is prima facie obvious over the prior art.

Conclusion

35 No claims are allowable.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (571) 272-0890. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M. IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, BRENDA BRUMBACK, CAN BE REACHED ON (571)272-0961.

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IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE FOLLOWING TC 1600 BEFORE AND AFTER FINAL RIGHT FAX NUMBERS:

BEFORE FINAL (703) 872-9306

AFTER FINAL (703) 872-9307

CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (571) 273-0890.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.



DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

DSR
SEPTEMBER 6, 2004